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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,388	01/10/2001	Juha Punnonen	0154.310US	2485

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,388	PUNNONEN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,35,37-41,52-57,59,68,70-76 and 79-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *33,35,37-41,52-57,59,68,70-76 and 79-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 33, 35, 37-41, 52-57, 59, 68, 70-76, and new Claims 79-97 are pending and being acted upon.

2. In view of Applicant's amendment and remarks, filed 10/06/03, only the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 59 and newly added Claim 97 stands/is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record as set forth in the paper mailed 5/05/03.

Applicant's arguments, filed 10/06/03, have been fully considered but they are not persuasive. Applicant argues a similar rejection to previous claims drawn to a vaccine. Much like vaccine claims, claims drawn to "a pharmaceutical composition" require relevant *in vivo* or *in vitro* enablement.

Applicant argues "contrary to these assertions [of lack of enablement], at the time the application was filed, conventional dendritic cell-based immunotherapies were in wide use in a variety of clinical trials and animals studies and commonly employed in a range of *in vivo* therapeutic approaches as vaccines against a number of diseases, including cancers and viral diseases."

While Applicant's assertions may be true, the cells of the instant claims are *not* conventional DCs. It is precisely because they differ from conventional DCs that they are not rendered obvious by conventional DCs. In particular, conventional DCs are known and under study for the treatment of cancers and viral diseases because of their ability to induce a Th1 type response. The cells of the instant claims are asserted to induce a Th2 type response. Applicant has provided insufficient evidence regarding

the efficacy in the treatment of cancers and viral diseases of a cell that induces a Th2 response to be considered enabling as a pharmaceutical composition.

Further regarding the specification's lack of an enabling disclosure, Applicant argues "The specification provides a clear description as to how to make and used [*sic*] the claimed cells and compositions in, for example, *in vivo* and *ex vivo* applications. See the specification, including at, e.g., at [*sic*] p. 41, line 7 to p. 49, line 36."

A review of the specification shows that pages 41-49 disclose no actual use of the cells of the instant claims but only prophetic, asserted uses of said cells.

Applicant argues "As with conventional dendritic cells, one of skill would consider the *in vitro* studies of the functional properties of the novel dendritic cells of the invention to be reasonably predictive of functional properties of these cells in *in vivo* or *ex vivo* applications."

Applicant is advised that relevant *in vitro* studies would be considered reasonably predictive of functional properties of the cells of the instant claims, however, a single MLR experiment is insufficient. Applicant is also again reminded that the DCs of the instant claims are *not* the conventional DCs of the prior art; Applicant has provided no basis for the assertion that the results of studies with conventional DCs can be extrapolated to predict the functional properties of the mDC2 cells of the instant claims.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 33, 35, 37-41, 52-57, 59, 68, 70-76 and newly added Claims 79-82, 85-89, 91-94, and 96-97 are/stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by EP 0808897 (1997, IDS), for the reasons of record as set forth in the paper mailed 5/05/03.

Applicant's arguments, filed 10/06/03, have been fully considered but they are not persuasive. Applicant argues "To establish a *prima facie* case of anticipation, it must be shown that each and every element as set forth in the claim is disclosed, either expressly or inherently, in the single cited prior art reference."

It is the Examiner's position that most of the limitations recited in the instant claims comprise limitations inherent to dendritic cells (DCs), e.g., lacking IL-12 production and CD14 expression, or expressing CD33 (see *Fundamental Immunology*, page 558). Specifically note the new limitation in the independent claims that the claimed cells "substantially lack CD14 surface marker expression." It is well-known in the art that CD14 is considered to be a macrophage marker which is not expressed on DCs. Note that the reference teaches that up to about 80% of the cells of the reference are CD14- (page 3, line 49). Accordingly, the recitation of this new limitation does not distinguish the DCs of the instant claims from the DCs of the prior art.

Applicant argues "The EP '897 application discloses macrophages -- not dendritic cells --that are substantially devoid of CD1a. The EP '897 application expressly states that macrophages are not dendritic cells. See, e.g., p. 2, lines 38-45."

A review of p. 2, lines 38-45 of the document shows no such "express statement". Additionally, the reference defines macrophages as the cells set forth by Metchnikoff in 1905, i.e., cells capable of phagocytosis and the secretion of immunoeffector monokines (page 2). Said definition encompasses DCs. Further, at the time of the reference the terms "macrophage" and "monocyte" were often used interchangeably, (*Fundamental Immunology*, page 558, column 2). Thus, the "monocyte derived antigen presenting cells (page 60) of the reference are the cells of the instant claims.

7. The following are new grounds for rejection.

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 33, 35, 37-41, 52-57, 59, 68, 73-76, and new Claims 79-87 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims

are directed to a monocyte-derived DC and a population of monocyte-derived DCs. As written, the claims read on cells comprising a human being. A human being is not-statutory subject matter. See 1077 O.G. 24, April 21, 1987.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 70 and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase "a population of cells...having a cytokine profile that differs from the cytokine profile of dendritic cells produced by ..." in Claim 70 is vague and indefinite as the phrase is not defined in the specification. Accordingly, the metes and bounds of precisely which cells would be encompassed by the claim cannot be determined.

12. Claims 33, 35, 37-41, 52-57, 59, 68, 70-76, and new Claims 79-97 and are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Ito et al. (1999)

Ito et al. teaches an APC identified as being devoid of surface CD1a (see particularly page 1415, column 2, ***Fraction 3*** and ***Fraction 2***). as set forth above, the additional limitations of the claims comprise only further characterization of the claimed cell type, e.g., a cell that substantially lacks IL-12 production. These properties are inherent to the cell of the reference. Some claims, e.g., Claim 38, recite product-by-process limitations, e.g., a differentiated cell cultured in Yssel's medium. Absent a showing that the process results in a novel product, said process is irrelevant. Further note that the source of the cells, i.e., monocyte derived, is also irrelevant absent a showing that said source provides novel properties. In the instant case, no such showing has been made. Accordingly, the cells of the reference are the cells of the instant claims.

The reference clearly anticipates the claimed invention.

Note that Applicant argues a similar rejection to previous claims. Applicant argues that "the rejection is nevertheless overcome by the Declaration of Juha Punnonen and Chia-Chun J. Chang Under 37 CFR j 1.131, which is attached hereto. This

declaration sets forth facts demonstrating the inventors reduced the claimed invention to practice in the United States prior to the August 1999 publication date of Ito.

Applicant has submitted a declaration by Inventors Punnonen and Chang comprising only what appear to be undescribed FACS plots taken from Inventor Chang's notebooks. Absent any explanations as to just what the raw data demonstrates, said data alone is insufficient to demonstrate that Applicant had reduced the claimed invention to practice in the United States prior to the August 1999.

13. Claims 33, 35, 37-41, 52-57, 59, 68, 70-76, and new Claims 79-97 and are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Rissoan et al. (1999)

Rissoan et al. teaches an APC identified as substantially lacks IL-12 production that induce Th2 differentiation (see particularly page 1183, column 3, and page 1184, column 3). As set forth above, the additional limitations of the claims comprise only further characterization of the claimed cell type, e.g., being devoid of surface CD1a. These properties are inherent to the cell of the reference. Some claims, e.g., Claim 38, recite product-by-process limitations, e.g., a differentiated cell cultured in Yssel's medium. Absent a showing that the process results in a novel product, said process is irrelevant. Further note that the source of the cells, i.e., monocyte derived, is also irrelevant absent a showing that said source provides novel properties. In the instant case, no such showing has been made. Accordingly, the cells of the reference are the cells of the instant claims.

The reference clearly anticipates the claimed invention.

Note that Applicant argues a similar rejection to previous claims. Applicant argues that "the rejection is nevertheless overcome by the Declaration of Juha Punnonen and Chia-Chun J. Chang Under 37 CFR 1.131 attached hereto. This declaration sets forth facts demonstrating the inventors reduced the claimed invention to practice in the United States prior to the February 19, 1999 publication date of Rissoan."

Applicant has submitted a declaration by Inventors Punnonen and Chang comprising only what appear to be undescribed FACS plots taken from Inventor Chang's notebooks. Absent any explanations as to just what the raw data demonstrates, said data alone is insufficient to demonstrate that Applicant had reduced

the claimed invention to practice in the United States prior to the February 19, 1999.

Applicant further argues "No evidence is provided that any dendritic cell disclosed in Rissoan substantially lacks expression of CD1a surface marker."

The reference teaches DC2 which induce Th2 differentiation as do the cells of the instant claims. Accordingly, it remains the Examiner's position that the instant specification provides nothing more than further characterization of the cells of the prior art.

14. Claims 33, 35, 37-41, 52-57, 59, 68, 70-76, and new Claims 79-97 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a monocyte-derived dendritic cell or composition thereof... "that substantially lacks CD14 surface marker expression" (Claims 33, 52, 68, 7072, 73, 88).

B) a monocyte-derived dendritic cell or composition thereof... "that express the CD83 surface marker" (Claims 79, 81, 83, 84, and 86).

C) a monocyte-derived dendritic cell that expresses at least one surface marker selected from the group of CD11c, CD33, and CD13" (Claims 80, 82, and 85).

D) a dendritic cell that "induces production of IL-6 or IL-8 in an amount comparable to that induced by a conventional dendritic cell" (Claim 87).

Applicant's remarks, filed 10/06/03, indicates that support for the amended claims in A) can be found at pages 53 and 55. First, it is noted that whereas page 53 disclosed "CD14- dendritic cells" and page 55 discloses DC with "strongly downregulated expression of CD14", neither cite discloses DC that "substantially lacks CD14 surface marker expression" as claimed. Regarding A), B), C), and D), it is noted that all cites are found in specific examples and not in generic disclosures regarding the cells of the instant claims. Thus, Applicant has improperly attempted to claim specific limitations set forth only in specific examples in the more generic claims now pending.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Please Note: inquiries of a general nature or relating to the status of this application should not be directed to the Examiner but rather should be directed to the Technology Center 1600 Customer Service Center at (703) 308-0198.

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600

1/6/03
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER